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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF:	:	
Patricia KANNOUCHE, et al.	: GROUP ART UNIT: 1634	
SERIAL NO.: 09/555,529	:	
FILED: JULY 24, 2000	: EXAMINER: JOHANNSEN	

FOR: SEQUENCES CODING FOR KIN17 PROTEIN AND THEIR APPLICATIONS

RESPONSE TO RESTRICTION REQUIREMENT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Responsive to the Official Action dated July 8, 2002, Applicants elect, with traverse, Group I, Claims 1-5, 24-25, and 29, for further prosecution.

REMARKS

The Office has required restriction in the present application as follows:

Group I: Claims 1-5, 24-25, and 29, drawn to nucleic acids encoding proteins and fragments thereof, including expression vectors, and nucleic acid detection reagents;

Group II: Claims 6-12, drawn to methods for detecting nucleic acids;

Group III: Claims 13-15 and 18-19, drawn to proteins;

Group IV: Claims 16-17, drawn to antisense oligonucleotides;

Group V: Claims 20-23, drawn to methods for preparing medicinal products using proteins or protein fragments;

Group VI: Claim 26, drawn to methods for preparing medicinal products using expression vectors;

Group VII: Claim 27, drawn to methods of detecting DNA repair using expression vectors; and

Group VIII: Claim 28, drawn to methods of regulating the "protein-curved DNA interaction" using a protein fragment.

Applicants elect, with traverse, Group I, Claims 1-5, 24-25, and 29, for further prosecution.

Applicants submit that the claims of Group V depend directly from the claims of Group III, and as such these claims can not be separated.

The Examiner, citing PCT Rule 13.1 and 13.2, contends that a lack of unity exists between Groups I-VIII, because the special technical feature of the present invention -the mammalian Kin17 protein- does not define a contribution over the prior art. To support this assertion the Office cites Kannouche et al (Biochimie 79(9-10):599-606) as disclosing the nucleic acids of Group I. However, Applicants submit herewith a statement from the publisher (Elsevier) stating that this reference "reached subscriber in the first week of January, 1998" and that "Elsevier received the issue 3-01-1998." Applicants note that the foreign priority date of the present application is December 9, 1997. Therefore, it is believed that, although it is dated October 1997, this reference should not be considered "prior art" on the basis of the January 1998 availability. Applicants submit that any further documentation necessary to support this position shall be provided as needed.

Accordingly, Applicants respectfully traverse the Restriction Requirement on the ground that unity of invention does exist between Groups I-VIII, because there is a technical relationship that involves the same special technical feature. It is this technical feature that defines the contribution which each of the Groups, taken as a whole, makes over the prior art.

Applicants traverse the Restriction Requirement on the additional grounds that the Office has not applied the same standard of unity of invention as the International

Preliminary Examination Authority. The Authority did not take the position that unity of invention was lacking in the International application and examined all claims together (see the International Preliminary Examination Report appended herewith). Applicants note that PCT Article 27(l) states that no national law shall require compliance with requirements relating to the form and contents of the International application different from or additional to those which are provided for in the Patent Cooperation Treaty and the Regulations.

Moreover, the MPEP in §803 states as follows:

> "If the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions."

Applicants respectfully submit that a search of all the claims would not impose a serious burden on the Office. In fact, the International Searching Authority has searched all of the claims together.

Applicants respectfully submit that the above-identified application is now in condition for examination on the merits, and early notice of such action is earnestly solicited.

Respectfully submitted,

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Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BLOcp263/35P	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR98/02667	International filing date (*day/month/year*) 09 December 1998 (09.12.98)	Priority date (*day/month/year*) 09 December 1997 (09.12.97)
International Patent Classification (IPC) or national classification and IPC C12N 15/12		
Applicant COMMISSARIAT A L'ENERGIE ATOMIQUE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25 June 1999 (25.06.99)	27 March 2000 (27.03.2000)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR98/02667

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☐ the international application as originally filed.

☒ the description, pages 1-33, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-29, filed with the letter of 21 February 2000 (21.02.2000),
Nos. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1/25-25/25, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR98/02667

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed.

   ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

See Separate Box

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: II

Priority

3. Additional observations:

The priority document relating to the present application was not available during the writing of this report. Consequently, the present application has been examined on the assumption that all the claims enjoy a priority date as of the filing date of the priority document (9 December 1997). Should it come to light that this is not the case the following document cited in the International Search Report could become relevant for establishing whether the subject of the present application fulfils the requirements of PCT Article 33(1) and 33(2).

P. KANNOUCHE ET AL.: "The nuclear concentration of Kin17, a mouse protein that binds to curved DNA, increases during cell proliferation and after UV irradiation", CARCINOGENESIS, Vol. 19, no. 5, May 1998, pages 781-789.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR 98/02667

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 4-12, 15-23, 25-29	YES
	Claims	2, 3, 13-14, 24	NO
Inventive step (IS)	Claims	1, 4, 5, 8-12, 15-23, 26, 27, 29	YES
	Claims	2, 3, 6, 7, 13-14, 24, 25, 28	NO
Industrial applicability (IA)	Claims	1-29	YES
	Claims		NO

2. Citations and explanations

1. Reference is made to the following documents:

D1: P. KANNOUCHE ET AL.: "Overexpression of Kin17 protein forms intranuclear foci in mammalian cells", BIOCHIMIE, Vol. 79, no. 9-10, October 1997, pages 599-606.

D2: M.D. ADAMS ET AL.: " EST63674 jurkat T-cells V Homo sapiens cDNA5' end similar to zinc finger protein KIN17", EMBL DATABASE ENTRY HSZZ60420, ACCESSION NUMBER AA355283, 18 April 1997.

D3: FR-A-2 706 487 (COMMISSARIAT A L'ENERGIE ATOMIQUE), 23 December 1994, cited in the application.

D4: A. MAZIN ET AL.: "Kin17, a mouse nuclear zinc finger protein that binds preferentially to curved DNA", NUCLEIC ACIDS RESEARCH., Vol. 22, No. 20, 1994, pages 4335-4341, cited in the application.

D5: J. F. ANGULO ET AL.: "Identification and expression of the cDNA of KIN17, a zinc-finger gene located on mouse chromosome 2, encoding a new DNA-binding protein", NUCLEIC ACIDS RESEARCH., Vol. 19, 1991, pages 5117-5123, cited in the application.

D6: A. TISSIER ET AL.: "Molecular cloning and characterisation of the mouse Kin17 gene coding for a Zn-finger protein that preferentially recognizes Curved DNA", GENOMICS, Vol. 38, no. 2, 1 December 1996, pages 238-242.

Novelty (PCT Article 33(1) and 33(2))

1) D1 does not appear to have been distributed to all the journals' subscribers until after October 1997, however, it appears improbable that the journal dated October 1997 was only made public three months later and was not accessible, before this date, to at least some members of the "public"; the above-mentioned subscribers represent only a very small part of the "public". Therefore, D1, is considered to be part of the prior art.

The subject matter of Claims 2, 3, 13-14 and 24 is not novel for the following reasons:

2) Document D1 discloses a sequence of nucleic acids coding for the kin17 mouse protein truncated between residues 129-228 ($_{Mm}$kin17ΔHR) sub-cloned in pCMV. This deletion corresponds to the residues coding for the homologous recA protein region (cf. Figure 1 and page 600, "Materials and methods": Plasmid construction). Therefore the subject matter of Claims 2 and 3 is not novel.

3) Document D1 also describes the protein coded by $_{Mm}$kin17ΔHR(Δamino acids 129-228) and the expression thereof in HeLa cells (page 602, second column, lines 40-54 and page 603, first column, lines 5-16). Consequently, the subject matter of Claims 13 and 14 is not novel.

4) Document D1 describes the expression of the truncated kin17 mouse protein corresponding to SEQ ID no. 2, sub-cloned in a pCMV expression vector (page 600, "plasmid construction"). Consequently, the subject matter of Claim 24 is not novel.

5) SEQ ID no. 1 which codes for the functional human kin17 protein, the fragments thereof (SEQ ID no. 4-21 and 33) and also the form that is truncated between the amino acids 129-288 of the human protein (SEQ ID no. 3) are not described in the prior art. The methods of detecting the human kin protein using one of sequences 1-21 and 33 as a probe or primer are not described.

The use of fragments truncated between the amino acids 129-288 or the C-terminal amino acids of the murine and human protein to inhibit cell proliferation or in the preparation of a medication for fertility control or to bind themselves to curved DNA is not described in the prior art. Therefore, the subject matter of Claims 1, 4-12, 15-23 and 25-29 is novel over the documents cited in the International Search Report.

Inventive step (PCT Article 33(1) and 33(3))

6) D3, which is considered to be the closest prior art, discloses the sequences coding for the murine (page 3, lines 20-30 and page 6, lines 19-27) and human proteins (page 8, lines 25-33) and also fragments of said sequences.

The prior art differs from the present application by the modification of these sequences and the use of these modified sequences in order to inhibit cell

proliferation.

The problem is therefore that of modifying the human and murine sequences in order to obtain truncated forms of the protein which have the capacity of inhibiting cell proliferation.

The solution to this problem proposed by the present application is that of modifying the human sequence by deleting the part which is homologous with the RecA protein or the entire N-terminal portion so as to retain only the 300-350 nucleotides which code for the C-terminal part of the murine or human protein so as to inhibit cell proliferation.

6a) D1 discloses expression vectors containing the murine sequence deleted in the part homologous to the RecA protein "$_{Mm}$kin17ΔHR" (Δamino acids 129-228) and its expression in HeLa cells (page 602, second column, lines 40-54 and page 603, first column, lines 5-16). As the sequence for the homologous human sequence of KIN17 is already known (D3), this truncated form is not a simple transposition of the modifications already known, from the mouse kin17 protein, to the human homologue thereof, as an unexpected effect has been shown by the applicants for this particular fragment. The prior art does not disclose the cell proliferation inhibiting effect (page 33, Figure 16) of the truncated human fragment corresponding to SEQ ID no. 3 and 23. Consequently, in the light of D3 in combination with D1, the subject matter of Claims 4 and 15 involves an inventive step.

As the C-terminal fragment (SEQ ID no. 33-36, 25, 26) also has a cell proliferation inhibiting effect

(page 27) the subject matter of Claims 16-23 and 26 involves an inventive step over the prior art cited in the International Search Report. The use of an expression vector as a tool for visualising the sites of DNA repair progression does not appear to be described. Therefore, the subject matter of Claim 27 is inventive.

6b) The sequence coding for the human functional kin17 cannot be derived from the prior art. Therefore, the subject matter of Claims 1, 5, 8-12 and 29 involve an inventive step.

6c) The use of a murine sequence (SEQ ID no. 2) for detecting the genomic DNA or the RNA of human kin17 is not inventive as it has been shown to be possible in several documents such as, for example, in the Southern blots which use the probe of mouse kin17 (D3: Example 2; D5: Figure 5 and page 5121, second column, final paragraph of "The mouse KIN17 gene is on chromosome 2, Band A"; or D6: Figure 2); marking a probe is not inventive either. Furthermore, in light of the large number of different fragments (SEQ ID no. 1-21 and 33) which can be used as probes, the fragment would appear to be of little importance. Furthermore, it is not necessary to have a fragment coding for the functional protein to detect an mRNA, a fragment of reasonable homology is sufficient. Consequently, the subject matter of Claims 6 and 7 is not inventive.

6d) An expression vector coding for a fusion protein containing the kin17 protein or a fragment thereof is not inventive, given that this type of construction is standard practice in laboratory experiments and is therefore part of the general

knowledge in the field. No particular inventive step is required to sub-clone a known sequence into an expression vector, for example, SEQ ID no. 2 and to express said sequence as a fusion protein. Therefore, the subject matter of Claim 25 is not inventive over D3 and the general knowledge of the field.

6e) D4 describes that the kin17 protein preferentially binds to curved DNA (abstract). D1 discloses that the part which is homologous to the RecA protein is probably responsible for the binding of the kin17 protein to the DNA, it is therefore logical to use this fragment to regulate the protein-curved DNA interaction. Moreover, D4 suggests that the residues 71-281 are involved in binding to the curved DNA; a smaller fragment which corresponds more specifically to the region which is homologous with RecA could be used. This fragment is a variant of that described in D4 and does not confer any particular advantages thereon. Therefore, in the light of D3 in combination with D1 and D4, the subject matter of Claim 28 does not involve an inventive step.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1) a) The functional feature "in that it is capable of expressing a functional human kin17 protein" of Claim 1, used to characterise sequence no. 1 is not based on the description (PCT Article 5) as the human protein coded by sequence no. 1 has not been tested and there is no proof that it is functional. As the difference between the plasmid of D3 and sequence no. 1 has not been described, it is difficult to appreciate what causes the protein of D3 to be non-functional and SEQ ID no. 1 to be functional. Moreover, should a person skilled in the art have all the tools required to obtain SEQ ID no. 1, and should Claim 1 fulfil the requirements of PCT Article 5, then the question is raised as to what causes it to be inventive.

b) Under the terms of PCT Article 5 it is not clear which function should be tested since, for the murine protein, for example, several different functions have been demonstrated and perhaps only some functions differentiate the protein described in D3 from that coded by SEQ ID no. 1. Furthermore, no function has been proved in the present application for the human protein.

2) Characterising a product by an arbitrary abbreviation without any real technical meaning does not appear to fulfil the requirements of PCT Article 6 in combination with PCT Rule 6.3. Therefore, the terms "kin17 protein" or "kin17ΔRH protein" used in the claims should either be defined

VIII. Certain observations on the international application

in known technical terms, such as, for example, an amino acid sequence, or should refer to a claim in which these terms are technically defined. This is the case, for example, in Claim 2, which does not refer to a particular sequence, although it is independent.

3) The region comprised in the "C-terminal part" is not clearly described. Therefore, the subject matter of Claims 19 and 21 is unclear under the terms of PCT Article 6. The description contains additional information (page 8, lines 4-6) which clarifies these terms; this is not the case in the present wording of Claims 16-18. As far as possible, the claims should be clear in themselves without requiring reference to the description.

4) The term "mammal" is broader than that which is effectively described in the description and the examples which describe only murine or human protein and not that of any other mammal. Therefore the subject matter of Claims 16, 20-22, 28 and 29 are not based on the description as required by PCT Article 6.

7) The use of the kin17 protein for preparing a fertility drug is not described in the description. Therefore, Claim 25 is not sufficiently supported by the description, as required by PCT Article 6. Since no example, either *in vitro* or *in vivo* even allows such an effect to be extrapolated, the scope thereof is broader than that which is justified by the description and the drawings.

8) The term "particularly", used in Claim 21, does not

VIII. Certain observations on the international application

introduce a limiting effect to the scope of the claim, thus the feature which follows such an expression should be considered to be entirely optional (PCT Article 6). The same comment applies to "optionally" used in Claim 29.

Additional observations:

The applicants' attention is drawn to the fact that, in light of the objections relating to novelty raised above (see Box V of the present preliminary opinion) it is possible that the claims which are considered to be novel are not so linked as to form a single general inventive concept and therefore do not fulfil the requirements of unity of PCT Rule 13.1.